L10: Entry 3 of 4 File: USPT Nov 21, 2000

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**** See image for Certificate of Correction ****
TITLE: Laser/sensitizer assisted immunotherapy

Brief Summary Text (19):
United States patents related to PDT include U.S. Pat. Nos. 5,095,030 and 5,283,225 to Levy et al.; U.S. Pat. No. 5,314,905 to Pandey et al.; U.S. Pat. No. 5,214,036 to Allison et al; and U.S. Pat. No. 5,258,453 to Kopecek et al., all of which are incorporated herein by reference. The Levy patents disclose the use of photosensitizers affected by a wavelength of between 670-780 nm conjugated to tumor specific antibodies, such as receptor-specific ligands, immunoglobulins or immunospecific portions of immunoglobulins. The Pandey patents are directed to pyropheophorbide compounds for use in standard photodynamic therapy. Pandey also discloses conjugating his compositions with ligands and antibodies. The Allison patent is similar to the Levy patents in that green porphyrins are conjugated to lipocomplexes to increase the specificity of the porphyrin compounds for the targeted tumor cells. The Kopecek patent also discloses compositions for treating cancerous tissues. These compositions consist of two drugs, an anti-cancer drug and a photoactivatable drug, attached to a copolymeric carrier. The compositions enter targeted cells by pinocytosis. The anti-cancer drug acts after the targeted cell has been invaded. After a period of time, a light source is used to activate the photosensitized substituent.

Drawing Description Text (4):
FIG. 3 is a chart showing tumor burden over time for untreated secondary tumors in the murine subject of FIG. 1.

Drawing Description Text (5):
FIG. 4 is a chart showing tumor burden over time for untreated secondary tumors in the murine subject of FIG. 2.

Detailed Description Text (37):
Immediately after laser treatment, all the tumors showed a slower growth within the first few days, then returned to a normal growth rate. Often the tumors would be partially bitten or chewed, but that would not stop or slow the tumor growth. Most rats died around 30 to 35 days except for the rats listed in Table II. About half the treated rats later developed secondary tumors, most as "hand bags" (metastatic to lymph nodes in the axillary region); the local expansions around the primary tumors were also in lymph nodes. In either case, the secondary tumors continued to grow until death occurred, except for the rats in Table II.

Detailed Description Text (41):
The secondary tumors of Srat1 and Srat2 appeared around day 20 after tumor transplant, and went through the same pattern as the primaries--growth/shrinkage/growth, as shown in FIGS. 3 and 4. In the case of Srat2, the recurrence of secondary tumors was almost negligible.

Detailed Description Text (42):
The tumor growth of three other rats is shown in FIG. 5. Srat3 and Srat6 started with only one primary tumor and Srat4 with two. FIG. 5 shows a much earlier response: tumor reduction started around 20 to 25 days. Furthermore, there are so far no secondary tumors, and the primary tumors have become only a small hard core of fibrous tissue; just a remnant of the tumor. Further development will be observed since all three remain alive at this time (Apr. 1, 1995).

Detailed Description Text (55):
The generation and acceleration of the immunological defense system response is further supported by the evolution of the secondary tumors of the long surviving rats. The metastasis usually occurred to half the rats around 15 to 20 days after the transplantation of primary tumors. The secondary tumors appeared in most cases along the milk lines and continued to grow until death. However, the metastatic tumors of Srat1 and Srat2 in FIGS. 3 and 4 showed exactly the same trend as in the primaries (FIGS. 1 and 2), with neither ICG-Chitosan injection nor laser treatment. FIG. 5 depicts the growth of primary

tumors of three rats (Srat3, Srat4 and Srat6), all of them following the same development--growth/treatment/growth/reduction. Furthermore, these three rats developed their full responses earlier; the tumor growth was stopped around 20 to 25 days after tumor transplantation and secondary tumors never appeared. This early establishment of the induced immunological defense mechanism may explain why these rats are still alive and have no signs of tumor recurrence.